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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/525,883

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Ursula Giesen

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EXAMINER

WHITE, DENNIS MICHAEL

ART UNIT

PAPER NUMBER

1797

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/525,883	GIESEN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	DENNIS M. WHITE	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 24 February 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>02/24/2005, 10/17/2005</u> .                                  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-22 and 27 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claims 1-22 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: Introducing the sample containing an analyte to come into contact with the metal complex.

### ***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-4, 6, 8-10, 13-16, 23, 26-28 are rejected under 35 U.S.C. 102(e) as being anticipated by Kumar et al (US 2004/0090168 and provisional application 60/390816).

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Regarding claims 1-4, 9-10, 15-16, 23, 26-28, Kumar et al teach a method and apparatus for detecting an analyte in a sample using a luminescent metal complex, such as Ru(II)(bpy)<sub>3</sub> substituted with functional groups that are used for linking the label to biomolecules (Pg. 14 lines 18-24), as a labelling group, comprising (i) oxidizing the metal complex an applied potential of 1.0-1.8V vs. Ag/AgCl (Pg. 16 lines 4-18), (ii) introducing hydrogen gas ("nascent hydrogen", hydrogen gas inherently reduces the metal complex by nascent hydrogen to produce a form of the metal complex that is capable of chemiluminescing) by applying a -1.5V (Pg. 17 lines 1-11); and (iii) assaying the ECL labeled biomolecules that are bound through biospecific interactions to binding reagents on the surface of the particles ("determining the analyte by means of the chemiluminescence") using a light detector (pg. 7 lines 1-7 and 17 lines 18-24).

Regarding claim 6, Kumar et al teach the metal complex binds to the analyte ("metal complex is used as a conjugate with a detection reagent for the analyte") (Pg. 17 lines 18-24).

Regarding claim 8, Kumar et al teach an assay using magnetic beads ("detection is carried out as a heterogeneous test") (Pg. 19 line 2).

Regarding claim 13, Kumar et al teach the reduction is separated in time from the oxidation by the introduction of the hydrogen gas after the oxidation potential (Pg. 17 lines 1-5).

Regarding claim 14, Kumar et al teach the generating of hydrogen at the electrodes ("the nascent hydrogen is generated in the direct vicinity of the metal complex") (Pg. 17 lines 1-7).

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar et al (2004/0090168) in view of Josel et al (USP 5,958,783).

Regarding claim 5, Kumar et al teach that the Ru(II)(bpy)<sub>3</sub> can be substituted with functional groups. Kumar et al are silent about the metal complex contains at least one hydrophilic group or/and a charge carrier.

Josel et al (USP 5,958,783) teach metal complexes such as Ru(II)(bpy)<sub>3</sub>-X, where the X is a charged linkers bound to one of the bipyridiyl ligands (col. 1 line 55-col. 2 line 39). Josel et al disclose it is advantageous to introduced a free positive or/and negative charge carriers into the linker which links the reactive coupling group of the metal complex to one of the ligands because it reduces the adsorption of conjugates of these complexes with an immunologically reactive substance and thus also improves the stability and recovery of the conjugates in immunoassays. Moreover an increased quantum yield can be achieved (col. 1 lines 44-52).

Therefore it would have been obvious to one of ordinary skill in the art as motivated by Josel et al to combine a charged linker to the metal complex of Kumar et al in order to reduce the adsorption of conjugates of these complexes with an immunologically reactive substance and improve the stability and recovery of the conjugates in immunoassays so that an increased quantum yield can be achieved.

10. Claims 7, 11-12, 21, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar et al in view of Bard et al (USP 5,714,089).

Regarding claim 7, Kumar et al teach an assay using magnetic beads ("detection is carried out as a heterogeneous test") but is silent about the assay is carried out as a homogeneous test.

Bard et al teach a method of use of ruthenium-containing and osmium-containing labels in binding methods for determining the presence of substances of interest. These methods may be used to determine labeled moieties of interest, to employ labeled moieties to determine analytes of interest, or to use labelled analogues of analytes of interest to determine analytes of interest in competitive binding assays. These binding methods may be homogeneous or heterogeneous binding methods. It is advantageous to use homogenous methods because binding of the analyte to the chemical moiety can directly influence the signal detectable from the label and there is no need for a filtering step.

Therefore it would have been well known to one of ordinary skill in the art to perform the heterogeneous method of Kumar et al with the homogenous method of Bard because the homogenous method does not require a step of filtering.

Regarding claims 11-12, 21, and 25, Kumar et al teach the oxidation of the metal complex electrochemically using electrodes but is silent about the metal complex is oxidized chemically by  $\text{PbO}_2$ , permanganate,  $\text{Ce}^{4+}$  compounds or/and peroxodisulfate.

Bard et al teach that  $\text{Ru}(\text{bpy})_3$  can be oxidized by either chemically by  $\text{PbO}_2$  or  $\text{Ce}^{4+}$  compounds or electrochemically. (col. 4 lines 31-48). It is known that these are equivalent methods for oxidizing the metal complex in electrochemiluminescence.

Therefore it would have been obvious to one of ordinary skill in the art as motivated by Bard et al to oxidize the metal complex of Kumar et al with  $\text{PbO}_2$  or  $\text{Ce}^{4+}$  compounds because they are known as equivalent methods to oxidize the metal complex in electrochemiluminescence assays.

11. Claims 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar et al in view of Harris et al (USP 4,842,844).

Kumar et al teaches claims 1-2 as per above.

Regarding claims 17-18, Kumar et al teach the generation of hydrogen gas using electrodes. Kumar is silent about the hydrogen is generated chemically by Li/butanol/H<sub>2</sub>SO<sub>4</sub>, Zn-Cu/ethanol or Zn/HCl.

Harris teaches a method of generating hydrogen by reacting hydrochloric acid and zinc. It is well known in the art that generating hydrogen chemically using Zn/HCl is a known equivalent method to using electrochemical methods.

Therefore it would have been obvious to one of ordinary skill in the art to substitute the method of generating hydrogen gas using an electrode of Kumar with the well known method of generating hydrogen gas using Zn/HCl of Harris et al in order to generate hydrogen gas.

12. Claims 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar in view of Riesz et al (Environmental Health Perspectives Vol. 64, pp. 233-252, 1985)

Regarding claims 19-20, Kumar et al teach the generation of hydrogen gas using electrodes in water. Kumar is silent about the hydrogen is generated by means of ultrasound that takes place by abstraction of hydrogen radicals from organic compounds and in particular from alkyl compounds.

Riesz et al teach the method of using ultrasound in aqueous solutions to generate hydrogen. It is well known in the art that generating hydrogen using ultrasound is a known equivalent method to using electrochemical methods.

Therefore it would have been obvious to one of ordinary skill in the art to substitute the method of generating hydrogen gas using an electrode of Kumar with the well known method of generating hydrogen using ultrasound in order to generate hydrogen in an aqueous solution.

13. Claims 22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar et al in view of Welk (CA 2313144 A1).

Regarding claims 22 and 24, Kumar teaches the oxidation and reduction potentials are alternated (Pg. 17 line 10) and the electrodes can be positioned in separate regions (Figure 2A-2J). Kumar is silent about the oxidation and generation of nascent hydrogen take place in two separate reaction chambers.

Welk teaches an electrolytic cell for the generation of nascent hydrogen and oxidizing agents wherein there are separate chambers for the positive and negative electrodes (abstract). It is desirable to keep the oxidation and reduction chambers separate in order to make sure the oxidizing agents do not react with the reducing agents and the metals are completely oxidized before being reduced.

Therefore it would have been obvious to one of ordinary skill in the art to modify the method and device of Kumar with the separate oxidation and reduction chambers of

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Well in order to to make sure the oxidizing agents do not react with the reducing agents and the metals are completely oxidized before being reduced.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DENNIS M. WHITE whose telephone number is (571)270-3747. The examiner can normally be reached on Monday-Thursday, EST 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

dmw

/Jill Warden/  
Supervisory Patent Examiner, Art Unit 1797